ORIGIO a CooperSurgical Company

APR 16 2014

K-133707 – SAGE 1-Step™

510(K) SUMMARY

Summary of Safety and Effectiveness Information
Supporting a Substantially Equivalent Determination

Submitted by: ORIGIO a/s
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Date Submitted: April 10, 2014

Device Identification
Trade name: SAGE 1-Step™ supplemented with Human Serum Albumin
SAGE 1-Step™ supplemented with Serum Protein Supplement

Common name: SAGE 1-Step™

Classification name: Reproductive media and supplements (21 CFR 884.6180, Product Code MQL)

Predicate device:
LifeGlobal: LifeGlobal Global® Total® (K112083).

Description
The SAGE 1-Step™ medium is intended for *in vitro* fertilization and culture of human gametes and embryos from fertilization until Day 5/6 of development. The medium can also be used for transfer.

Two versions of the SAGE 1-Step™ medium are available:

- Catalogue no. 6701: SAGE 1-Step™ supplemented with Human Serum Albumin
- Catalogue no. 6702: SAGE 1-Step™ supplemented with Serum Protein Supplement

Both versions of SAGE 1-Step™ are aseptically filtered, light pink, non viscous solutions, which are ready to use by professionals within assisted reproduction.

The SAGE 1-Step™ media products are contained in 10 ml or 60 ml transparent Polyethylene Terephthalate Glycol (PETG) bottles with high density polyethylene (HDPE) cap, available in a card board boxes of 1 x 10 ml and 1 x 60 ml bottles. The bottles are individually labeled. The boxes also contain instruction for use provided as package insert.

Compositions:
The different types of components included in SAGE 1-Step™ supplemented with Human Serum Albumin and SAGE™ 1 step supplemented with Serum Protein Supplement are provided in table 1.

Indication for use
This product is intended for *in vitro* fertilization and culture of human gametes and embryos from fertilization until Day 5/6 of development. The medium can also be used for embryo transfer.

Technological Characteristics
The design of the SAGE 1-Step™ as well as the predicate listed in this submission, are based on the concept to offer the embryos various components at any time, from fertilization until blastocyst stage. Table 1 compares the technological characteristics of SAGE 1-Step™ with the predicate Global® Total®. Both similarities and differences are illustrated.

SAGE 1-Step™ is for fertilization; culture and embryo transfer. Global® Total ® is intended for culture of human embryos from zygote to blastocyst and embryo transfer. In vivo the gametes and zygote are exposed to the same environment as the spermatozoa fertilizes the oocyte and forms the zygote in the part of the fallopian tube called the ampulla. Thus, the intended use for the SAGE 1-StepTM is considered comparable to the predicate and the differences are not considered to represent a new intended use nor does it pose any safety or effectiveness issues.

Table 1 Comparison of SAGE 1-Step™ with the predicate Global® Total®

Product	**SAGE 1-Step™ (REF 6701)**	**SAGE 1-Step™ (REF 6702)**	**Global® Total®**
Intended use	This product is intended for the *in vitro* fertilization and culture of human gametes and embryos from fertilization until Day 5/6 of development. The medium can also be used for embryo transfer.	This product is intended for the *in vitro* fertilization and culture of human gametes and embryos from fertilization until Day 5/6 of development. The medium can also be used for embryo transfer.	Culture of human embryos from zygote to blastocyst, and embryo transfer.
Product specification			
pH	7.2-7.4	7.2-7.4	7.2-7.4
Osmolality (mOsm/kg)	257-273	257-273	260-270
Endotoxin (EU/mL)	<0.15	<0.15	<0.50
Sterility	No growth	No growth	negative
1-cell MEA	≥80%	≥80%	>80%
Formulation			
Physiological salts	Magnesium Sulphate Potassium Chloride Potassium Phosphate Sodium Chloride	Magnesium Sulphate Potassium Chloride Potassium Phosphate Sodium Chloride	Calcium Chloride Magnesium Sulphate Potassium Chloride Potassium Phosphate Sodium Chloride
Amino Acids	Yes	Yes	Yes

Product	SAGE 1-Step™ (REF 6701)	SAGE 1-Step™ (REF 6702)	Global® Total®
Stable form of L-Glutamine	Alanyl-Glutamine	Alanyl-Glutamine	Glycyl-Glutamine
Energy sources	Glucose Calcium-L-Lactate Sodium Pyruvate	Glucose Calcium-L-Lactate Sodium Pyruvate	Glucose Sodium-DL-Lactate Sodium Pyruvate
EDTA	Yes	Yes	Yes
Buffer	Sodium Bicarbonate	Sodium Bicarbonate	Sodium Bicarbonate
Phenol Red	Yes	Yes	Yes
Sodium hyaluronate	0.1 mg/mL	-	-
Protein source			
HSA (proteins: albumin)	5 mg/mL	-	-
PPF (proteins: albumin,α- and β-globulins)	-	5 mg/mL	-
LGPS (proteins: albumin, α- and β-globulins)	-	-	5 mg/mL
Drugs			
Gentamicin sulphate	0.01 mg/mL	0.01 mg/mL	0.01 mg/mL

The base medium of SAGE 1-Step™, as well as the predicate, is similar to the first single-step medium developed by Lawitts and Biggers (1991) and later supplemented with amino acids.

The technological characteristics of SAGE 1-Step™ are comparable to those of the predicate device. The main differences are:

- Protein supplementation: SAGE 1-Step™ is available in two ready-to-use formulations with either Serum Protein Supplementation (REF 6702) or Human Serum Albumin (REF 6701) as protein source. The protein source of the predicate is LGPS which is similar to Serum Protein Supplementation as they both contain albumin and globulins. Human Serum Albumin is different from the protein source in the predicate, it is however a standard protein supplement used in other cleared devices for continuous culture such as Irvine Scientific Continuous Single Culture Complete (K121572).
- Sodium Hyaluronate: SAGE 1-Step™ supplemented with Human Serum Albumin is further added Sodium Hyaluronate as a supplement to albumin. Sodium Hyaluronate is a well known component in other ART media (VitroLifes G-series (K081114, K081117, K031015)) and hyaluronan is naturally found in the female reproductive tract. Thus the addition of Sodium Hyaluronate in SAGE 1-Step™ supplemented with Human Serum Albumin (REF 6701) is not considered to represent a new technology when compared to the predicate.
- Lactate: SAGE 1-Step™ contains Ca-L-Lactate whereas the predicate contains Na-DL-Lactate.. The concentration of L-lactate in SAGE 1-Step™ is comparable with the concentration of L-lactate in the predicate.
- Magnesium Sulphate is added in a higher concentration compared to the predicate. However other culture media e.g Quinn´s Advantage media (K002836) also contain higher concentrations of Magnesium Sulphate and it is judged that it will not influence the performance or safety compared to the predicate device .
- Calcium: Calcium is added in the form of Ca-Lactate whereas the predicate contains Na-Lactate. The Calcium concentration in SAGE 1-Step™ is similar to the predicate and therefore it has no impact.

- Stable L-Glutamine: Both SAGE 1-Step™ and the predicate contains a stable form of glutamine. Both Alanyl-Glutamine used in SAGE 1-STEP™ and Glycyl-Glutamine used in the predicate are widely used in ART media and have a history of safe use.

The differences in composition do not impact the substantial equivalence and do not raise any new types of safety or effectiveness concern.

Performance data
The product specifications for SAGE 1-Step™ and the predicate are similar regarding sterility, pH, and Mouse Embryo Assay (MEA) test. However, the endotoxin levels varies. Endotoxin is <0.50 EU/mL for Global® Total®. For SAGE 1-Step™ the endotoxin limit is <0.15 EU/mL.

Regarding the osmolality, the specification limit is a bit wider for SAGE 1-Step™ (257-273 mOsm/kg) than for the predicate (260-270 mOsm/kg).

The shelf life of SAGE 1-Step™ has been validated in stability studies to 14 weeks. The parameters which have been tested in the stability studies through shelf life includes pH, osmolality, endotoxin, HSA concentration, MEA, and sterility.

In general, SAGE 1-Step™ medium is subject to the same control methods and, to a significant degree, contain the same components as the predicate device. SAGE 1-Step™ has similar handling procedures and storage conditions. Therefore, SAGE 1-Step™ is considered substantially equivalent to the predicate device Global® Total®.

Biocompatibility
SAGE 1-Step™ is categorized as a medium in direct contact with gametes and embryos from fertilization till blastocyst stage. Since SAGE 1-Step™ can also be used for embryo transfer, it is also in direct contact with the uterus (patient). The biological safety evaluation (ISO 10993-1) demonstrates that SAGE 1-Step™ medium, consist of well tested components and is non-toxic in use. SAGE 1-Step™ is therefore considered safe for fertilization and culture of human gametes and embryos as well as transfer of embryos back into the patient (uterus).

Conclusion
The conclusion from the performance and safety data, intended use comparison, product formulation comparison, and test specification comparison, demonstrates that the SAGE 1-Step™ supplemented with Human Serum Albumin and SAGE 1-Step™ supplemented with Serum Protein Supplement are suitable for its intended use, and meets the criteria in the comparison to the predicate device LifeGlobal Global® Total® (K112083).

DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
10903 New Hampshire Avenue
Document Control Center – WO66-G609
Silver Spring, MD 20993-0002

April 16, 2014

ORIGIO a/s
Tove Kjaer
Director Corporate Regulatory Affairs
Knardrupvej 2
Måløv 2760
Denmark

Re: K133707
Trade/Device Name: SAGE 1-Step™ supplemented with Human Serum Albumin and SAGE 1-Step™ supplemented with Serum Protein Supplement
Regulation Number: 21 CFR§ 884.6180
Regulation Name: Reproductive media and supplements
Regulatory Class: II
Product Code: MQL
Dated: March 17, 2014
Received: March 19, 2014

Dear Tove Kjaer,

We have reviewed your Section 510(k) premarket notification of intent to market the device referenced above and have determined the device is substantially equivalent (for the indications for use stated in the enclosure) to legally marketed predicate devices marketed in interstate commerce prior to May 28, 1976, the enactment date of the Medical Device Amendments, or to devices that have been reclassified in accordance with the provisions of the Federal Food, Drug, and Cosmetic Act (Act) that do not require approval of a premarket approval application (PMA). You may, therefore, market the device, subject to the general controls provisions of the Act. The general controls provisions of the Act include requirements for annual registration, listing of devices, good manufacturing practice, labeling, and prohibitions against misbranding and adulteration. Please note: CDRH does not evaluate information related to contract liability warranties. We remind you, however, that device labeling must be truthful and not misleading.

If your device is classified (see above) into either class II (Special Controls) or class III (PMA), it may be subject to additional controls. Existing major regulations affecting your device can be found in the Code of Federal Regulations, Title 21, Parts 800 to 898. In addition, FDA may publish further announcements concerning your device in the Federal Register.

Please be advised that FDA's issuance of a substantial equivalence determination does not mean that FDA has made a determination that your device complies with other requirements of the Act or any Federal statutes and regulations administered by other Federal agencies.

You must comply with all the Act's requirements, including, but not limited to: registration and listing (21 CFR Part 807); labeling (21 CFR Part 801); medical device reporting (reporting of medical device-related adverse events) (21 CFR 803); good manufacturing practice requirements as set forth in the quality systems (QS) regulation (21 CFR Part 820); and if applicable, the electronic product radiation control provisions (Sections 531-542 of the Act); 21 CFR 1000-1050.

If you desire specific advice for your device on our labeling regulation (21 CFR Part 801), please go to http://www.fda.gov/AboutFDA/CentersOffices/CDRH/CDRHOffices/ucm115809.htm for the Center for Devices and Radiological Health's (CDRH's) Office of Compliance. Also, please note the regulation entitled, "Misbranding by reference to premarket notification" (21CFR Part 807.97). For questions regarding the reporting of adverse events under the MDR regulation (21 CFR Part 803), please go to http://www.fda.gov/MedicalDevices/Safety/ReportaProblem/default.htm for the CDRH's Office of Surveillance and Biometrics/Division of Postmarket Surveillance.

You may obtain other general information on your responsibilities under the Act from the Division of Small Manufacturers, International and Consumer Assistance at its toll-free number (800) 638-2041 or (301) 796-7100 or at its Internet address http://www.fda.gov/MedicalDevices/ResourcesforYou/Industry/default.htm.

Sincerely yours,

Benjamin R. Fisher -S

Benjamin R. Fisher, Ph.D.
Director
Division of Reproductive, Gastro-Renal,
and Urological Devices
Office of Device Evaluation
Center for Devices and Radiological Health

Enclosure

DEPARTMENT OF HEALTH AND HUMAN SERVICES
Food and Drug Administration

Indications for Use

Form Approved: OMB No. 0910-0120
Expiration Date: December 31, 2013
See PRA Statement on last page.

510(k) Number *(if known)*
K133707

Device Name
SAGE 1-Step™ with Human Serum Albumin and SAGE 1-Step™ with Serum Protein Supplement

Indications for Use *(Describe)*
These products are intended for the in vitro fertilization and culture of human gametes and embryos from fertilization until Day 5/6 of development. The media can also be used for transfer.

Type of Use *(Select one or both, as applicable)*

☒ Prescription Use (Part 21 CFR 801 Subpart D) ☐ Over-The-Counter Use (21 CFR 801 Subpart C)

PLEASE DO NOT WRITE BELOW THIS LINE – CONTINUE ON A SEPARATE PAGE IF NEEDED.

FOR FDA USE ONLY

Concurrence of Center for Devices and Radiological Health (CDRH) *(Signature)*

Benjamin R. Fisher -S
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